

While biotin and iminobiotin "A" moieties are the subject of the experimental examples, the properties required of "A" are described (pg. 12, lines 1-10: "A may be any moiety which has at least three carbon atoms and is capable of forming a detectable complex with a polypeptide when the modified nucleotide is incorporated into a double-stranded duplex..."). In addition, five specific moieties in addition to biotin and iminobiotin are named as options for "A" (pg. 12, lines 12-34). Applicants clearly teach that the lipoyl, benzoyl, succinyl, phthalic acyl and 2-(2,4 dinitro benzylamino) acetyl moieties disclosed on page 12 can be used in addition to biotin and iminobiotin in the invention. Therefore, one skilled in the art could easily select additional "A" moieties having similar properties without undue experimentation based on the teaching of the specification, the seven "A" moieties specifically disclosed and the many ligand pairs known in the art which are taught by such publications (copies enclosed) as U.S. Patent No. 4,067,774 (see columns 7-29) and British Patent No. 1 564 578 (see the paragraph spanning pages 5-6).

In view of these extensive teachings and the knowledge of one skilled in the art it is improper to require that the claims be limited only to "A" moieties specifically exemplified in experimental examples since it is not required that each claimed embodiment be supported by an experimental example. In re Borkowski, 164 USPQ 642 (CCPA 1970). It is therefore requested that the rejection be withdrawn.

B. Claims 104-109, 113-118, 125-137 and 140-144 are rejected as the disclosure is allegedly enabling only for specific linker groups which do not inhibit hybridization of the polynucleotide. Applicants traverse for the following reasons.

The disclosure of the present invention teaches that it is the position of attachment of the probe moiety on the ring which may adversely affect hydrogen bonding of the bases (p. 9, lines 11-26). There is considerable flexibility in the choice of linkers as long as the linker is attached to the ring at one of the positions which Applicants disclose as not adversely affecting hydrogen bonding (pg. 13, lines 10-32). Certain properties, such as an  $\alpha$ -olefinic bond, are preferred to enhance complex formation with the detectable polypeptide, but these are not required.

Therefore, although there are many possible useful linkers which fit Applicants' description, selecting them and attaching them to bases at particular sites on the ring as taught by Applicants involves no more than routine chemical procedures and an ordinary level of skill. Such routine screening, even though it may be time consuming, is not in itself evidence of undue experimentation. In re Wands, 8 USPQ 2d 1400 (CAFC 1988). Applicants respectfully request withdrawal of the rejection.

C. Claims 104-109, 113-118, 125-137 and 140-144 are rejected as the disclosure is allegedly enabling only for "bound" being hybridization. Although Applicants do not agree with the analysis, Claim 125 has been amended to correct the antecedent basis by substituting "hybridized" for "bound." This rejection is therefore moot and its withdrawal is requested.

Rejections Under 35 U.S.C. 112, second paragraph

A. Claims 104-109, 113-118, 125-137 and 140-144 are rejected as allegedly indefinite for the recitation of "it is attached" in Claim 125. By the present amendment "it" is replaced by the recitation "the sugar moiety." Applicants respectfully submit that this amendment establishes proper antecedent basis and

clarifies any alleged indefiniteness. Withdrawal of the rejection is therefore requested.

B. Dependency of Claim 113 has been corrected by the present amendment obviating the rejection based on its former dependence from cancelled claims.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that the present application is in condition for allowance. An action passing this case to issue is therefore requested.

Respectfully submitted,

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